

## REMARKS

Firstly, the Examiner is cordially thanked for the opportunity to discuss this case in a personal interview which was conducted at the PTO on November 21, 2002. During the course of the interview, all the pending claims were discussed with the major focus of discussion being on claim 1.

As discussed at the interview, neither Medof nor Tsuji anticipates the instant claims. The instant claims recite, *e.g.*, that the claimed glycoprotein comprises a "tumor-specific glycostructure," whereas the glycoproteins of Medof and Tsuji are both isolated from non-tumor tissue and do not comprise the recited tumor-specific glycostructure. The difference between the glycoproteins of the instant claims and the references is evidenced, *e.g.*, by their different molecular weights. The instantly claimed glycoprotein, which is isolatable from tumor cells, such as human adenocarcinoma cell lines 23132, 3051 or 2957, or primary tumor cells of gastric adenocarcinoma patients, has a molecular weight of about 82 kd. See, *e.g.*, the instant specification at page 5, lines 12-18. By contrast, the glycoproteins of the references are isolated from non-tumor cells (human blood cells) and exhibit molecular weights which are not 82 kD. In Medof, the glycoprotein is isolated from human red cells (see, *e.g.*, the sentence beginning at the last line of page 1558) and has a molecular weight on SDS-PAGE of 70,000 (see, *e.g.*, page 1560, last 6 lines of the section entitled "Purification and Characterization of DAF"; page 1562, second full paragraph; and Fig. 2). In Tsuji, as the Examiner admits, DAF is purified from (non-tumor) human blood. DAF has a molecular weight of 70 kd as disclosed at column 4, lines 5-8 of the Tsuji patent (US 5,695,945).

Further, as discussed at the interview, the Hensel reference (*Laboratory Investigations*, November 2001, Vol.81, no.11, pp.1553-1563) clearly discloses (at page 1554, column 2 and figure 1) that the antibody SC-1 reacts with the 82 kd protein on stomach cancer cells but not with the 70 kd form of the CD55 protein on HeLa cells.

Claim 1 now as amended recites that the isolated glycoprotein is an 82 kd glycoprotein. Applicants have provided further experimental data (see attachment), including Western blots and FACS analyses, which show that the SC-1 antibody reacts with the 82kd protein on a variety of different stomach carcinoma cell lines. In view of the present amendment, it is clear that claim

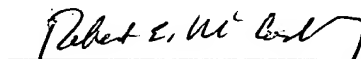
I which recites that the glycoprotein has a molecular weight of 82 kd meets the written description under §112, first paragraph. Especially claims 38 and 39 which recite that the glycoprotein is isolatable from specific cell types, e.g. human gastric carcinoma cells and a particular human adenocarcinoma cell line, as supported by the attached data. Moreover, the glycoprotein is naturally occurring as recited in claim 40.

In view of the above remarks and amendments, it is submitted that this application is now ready for allowance. However, if there are any remaining issues which can be resolved expeditiously by a telephone conference, the Examiner is courteously requested to telephone the undersigned at the number indicated below.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Attached hereto is a marked up version of the changes to the specification and claims by the current amendment. The attached pages are captioned "Version With Markings to Show Changes Made".

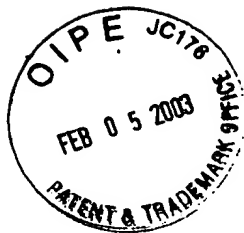
Respectfully submitted,



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**Date: February 5, 2003**



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**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

1. (Amended) An isolated glycoprotein that comprises at least one section of the amino acid primary structure of CD55 and a tumor-specific glycostructure and has a molecular weight of 82 kd, wherein the glycostructure reacts with monoclonal antibody SC-1



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## Expression of SC-1 specific CD55 isoform on different stomach carcinoma cell lines

### Aim of the study:

On the stomach carcinoma cell line 23132 an 82 kD isoform of CD55 was isolated which reacts with the apoptosis inducing antibody SC-1 (Hensel et al., Cancer Res., 1999). For further distribution study membrane preparations of stomach carcinoma cell lines 23132, 3051, 4433 and KATO III were prepared and subjected to Western blot analysis with the antibody SC-1 to test expression of the 82 kD isoform of CD55. To verify the expression of CD55<sup>SC-1</sup> on the membrane of different stomach carcinoma cells, the cell lines 3051, 2474 and 4433 were investigated in FACS analysis.

### Methods:

#### **Preparation of membrane extracts and Western blotting**

See Hensel et al., Cancer Res., 1999

#### **FACS analysis:**

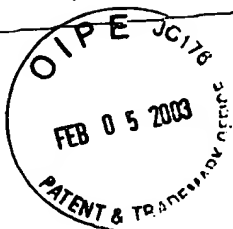
See Hensel et al., Lab. Invest., 2001

### Results:

Western blot analysis show the expression of the 82 kD isoform of CD55 as previously shown on cell line 23132 (Hensel et al., Cancer Res., 1999). These data show that the isolation of the SC-1 specific CD55 isoform is not only possible from the described cell line 23132 but also from different other stomach carcinoma cell lines. These data are confirmed by the FACS analysis with cell lines 3051, 2474 and 4433. The antibody SC-1 binds to all of these stomach carcinoma cell lines indicating an expression of CD55<sup>SC-1</sup> on the cell membrane.

### Conclusion:

The isolation of the 82 kD isoform of CD55 is possible from sources different from cell line 23132 and can therefore not be restricted to this in the patent.



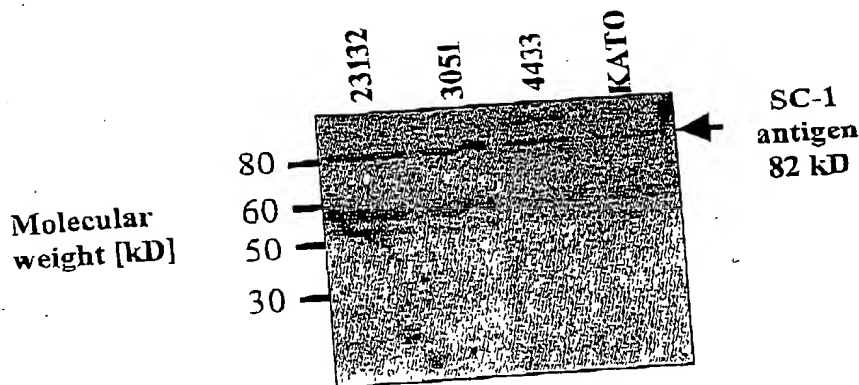
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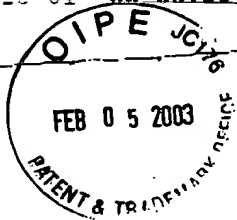
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Experimental data

Isolation of SC-1 receptor from different stomach carcinoma cell-lines

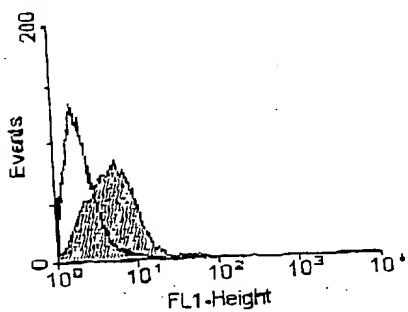




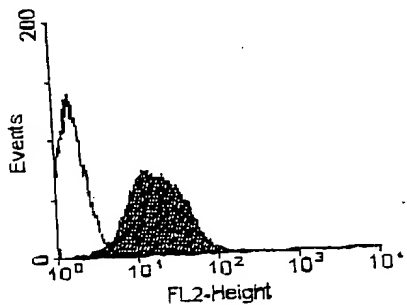
Detection of SC-1 receptor on different stomach carcinoma cell-lines by FACS analysis

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Cell-line 3051

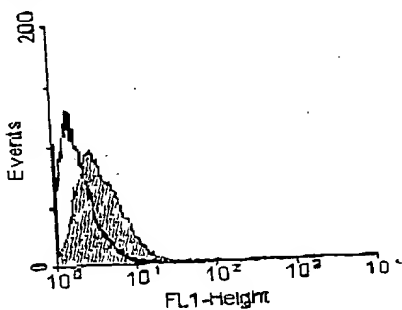


Antibody SC-1

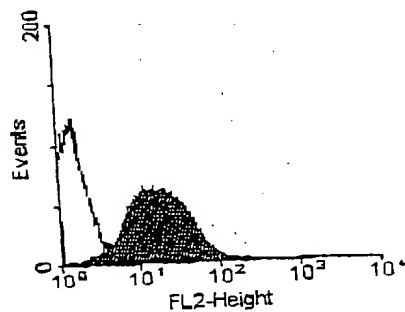


Antibody CD55

Cell-line 2474

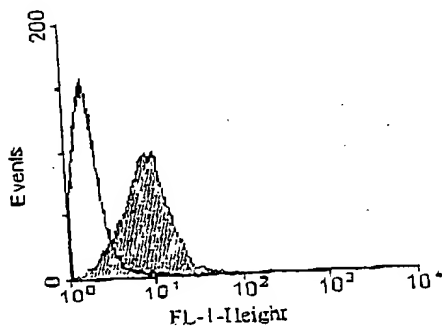


Antibody SC-1

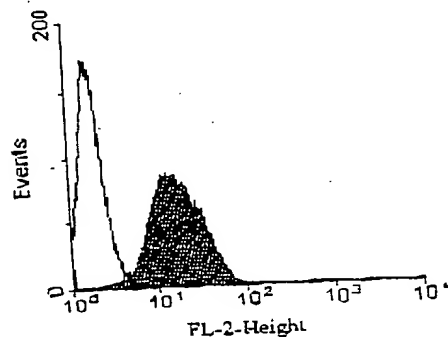


Antibody CD55

Cell-line 4433



Antibody SC-1



Antibody CD55